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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/559,021	04/27/2000	Alexander V. Sokoloff	Mirus.014.02	1870

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/559,021	SOKOLOFF ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 3/18/2004, in which claim 1 was amended and in which claim 5 was cancelled following incorporation of its limitations into claim 1. Additional claims were cancelled in the amendment filed 3/18/2004 (claims 2, 6, 8-16). Claims 1, 3-4 and 7 are pending in the instant application.

Any rejection of record in the previous office actions not addressed herein is withdrawn. New grounds of rejection are presented herein that were not necessitated by applicants' amendment of the claims since the office action mailed 2/10/2004. Therefore, this action is not final.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejected claims are directed to an *in vitro* method for selecting phage that are resistant to blood inactivation comprising mixing a blood component with a phage display library *in vitro* and selecting for phage that are resistant to inactivation by the blood component. Selection can comprise multiple rounds of selection and can involve identification of a variable sequence of the phage DNA. Applicants' disclose in their specification that they have used their phage display methods to identify peptides that bind to a complement C-reactive protein (i.e. CRP) and which prolong the blood circulation of T7 phage displaying the peptide by preventing

phage inactivation by complement (termed "C" in the instant specification; e.g. bridging paragraph for pages 21-22 of the instant specification).

Claims 1, 3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Sahu et al (Journal of Immunology, Vol. 157, No. 2, pages 884-891, 1996; see the entire reference). **This is a new rejection.**

Sahu et al teach the identification, isolation and characterization of a peptide that binds to a protein in the complement cascade pathway and inhibits both the classical and alternative pathways for complement activation (e.g. the Abstract; Table 1, see peptides I and IV; page 890, column 1, last paragraph). To identify their polypeptide, Sahu et al screened a phage-displayed *random* peptide library that contains 2×10^8 unique clones expressing C3b-binding peptides *in vitro* (e.g. first paragraph under results, page 886). After 3 rounds of selection, individual phage were isolated and tested for binding, with 14 of 16 clones binding to C3b. DNA was isolated from all 14 positive clones and each was found to encode an identical sequence (e.g. see Table 1, clone 9), indicating the clone was specific and had been amplified during the multiple rounds of selection.

The rational that the isolated phage bearing the polypeptide displayed by clone 9 (e.g. see Table 1) would have been resistant to inactivation by the complement component is based upon the reasonable expectation that such phage would necessarily inhibit complement activation such that phage bearing the peptide would retain the ability to infect the appropriate host cell. This is consistent with applicants' own observation that inhibition of complement activation by binding to CRP prolongs the half-life in the blood for phage bearing the CRP-binding polypeptide(s).

Therefore, absent any evidence to the contrary, the skilled artisan would necessarily expect upon reading the teachings of Sahu et al that phage bearing the peptide sequences taught by Sahu et al would be resistant to inactivation by C3 and the complement cascade.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sahu et al (Journal of Immunology, Vol. 157, No. 2, pages 884-891, 1996; see the entire reference) in view of the 1997 Novagen Catalog (Novagen, Inc. see pages 24-26 of the 1997 catalog). **This is a new rejection.**

The teachings of each of the Sahu et al references are described above and are applied as before, except:

The Sahu et al reference exemplifies the use of a filamentous phage display system. The Sahu et al reference does not explicitly teach the use of T7 phage in their methods of selecting for phage displaying a polypeptide that inhibits complement activation.

The 1997 Novagen catalog provides teachings concerning a "T7Select" phage display system that was well known and used in the art at the time of the instant invention (see pages 24-26 of the catalog). In particular, the catalog teaches several advantages of the T7 system, including ease of growth and high copy number for displayed peptides (e.g. the table labeled "Advantages" on page 24).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Sahu et al to include the T7 phage display system taught and sold by Novagen because Sahu et al teach it is within the skill of the art to use a population of phage displaying a plurality of variations of the coat polypeptides to select variants that demonstrate an ability to inhibit complement activation (e.g. by binding and inhibiting C3 of the complement cascade). It would have been obvious to make such a modification in order to receive any of the expected benefits recited in the teachings of the Promega cagalog with regard to using T7 phage display systems. In addition, or alternatively, one could reasonably expect to select for phage

having different display characteristics than the filamentous phage exemplified in the teachings of the Sahu et al reference, and/or a different range of target bacterial cells capable of infection by the phage. Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the teachings of Sahu et al to include the T7Select system taught by the Novagen catalog.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Gerald G Leffers Jr./
GERRY LEFFERS
PRIMARY EXAMINER

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636